

REMARKS

The Examiner has acknowledged Applicants' election of Group IV and species (c), (e), (f), and (h). Claims 8-9, 11-17, and 45-51 have been withdrawn as being drawn to a nonelected group. The Examiner, therefore, concludes that claims 1-7, 10, and 18-44 (Figure 4) are under consideration. For the sake of clarity, however, Applicants refer the Examiner to the Preliminary Amendment submitted at the time of filing in the United States, wherein amendments to the claims were presented, claims 11-17 and 35-38 were canceled, and new claim 51 was added. Accordingly, claims 1-7, 10, 18-34, and 39-44 (Figure 4) are under consideration.

Claims 1-4 and 7 have been amended to improve clarity and correct minor typographical errors. Claims 1 and 3 have been amended to clarify the numbering of the amino acid residues at positions I-IV of the first binding site. Specifically, claims 1 and 3 have been amended to replace recited residues "122, 54, 50 and 95" with residues "139, 71, 67, and 112". The discrepancy in numbering with regard to positions I-IV of the first binding site, which amounts to a consistent differential of 17 amino acids, stemmed from the difference in length observed between the full length protein, which comprises an N-terminal leader sequence, and the mature protein, from which the leader sequence has been processed or removed. SEQ ID NO: 4 which is presented in Figure 4 depicts the amino acid sequence of the full length protein. As a consequence, the numerical delineations of positions I-IV of the first binding site are, accordingly, shifted by 17 residues.

Claims 2 and 3 have been amended to clarify the numbering of the amino acid residues at positions I-IV of the second binding site. Specifically, claims 2 and 3 have been amended to replace recited residues "112, 149, 35 and 135" with residues "129, 166, 52 and 152". As set forth above with regard to positions I-IV of the first binding site, positions I-IV of the second binding site were originally presented with regard to the shorter, mature protein. As is evident from the specification and drawings, in particular Figures 4 and 22, positions I-IV of the second binding site correspond to residues 129, 166, 52 and 152 of the full length protein as shown in Figure 4. Support for the amendment to claims 1-3 is presented throughout the specification and in the Figures as indicated herein above.

Claim 4 has been amended to correct a clerical error. Claim 7 has been amended to

rectify a grammatical error. No new matter is introduced by these amendments.

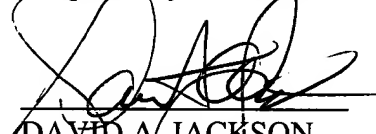
By this Office Action, the Examiner has required restriction within the formerly presented Invention of Group IV (claims 1-7, 10, 18-44; Figure 4). The Examiner contends that claims 1-7, 10, and 18-44 are drawn to numerous species. Specifically, the Examiner maintains that the claims of Invention IV pertain to eleven (11) species corresponding to each of SEQ ID Nos: 1-11.

Responsive to the Requirement for restriction, Applicants elect to prosecute the single species of SEQ ID NO: 4, which is set forth in Figure 4.

No additional fees are believed to be necessitated by the foregoing Response. However, should this be erroneous, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages.

In view of the above, withdrawal of the Requirement for the Restriction is requested, and an early action on the merits of the Claims is courteously solicited.

Respectfully submitted,

  
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**In the Claims:**

1. (currently amended). A histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than  $10^{-7}M$  and which has a binding site comprising amino acid residues phenylalanine, isoleucine or leucine at position I, tryptophan at position II and aspartate or glutamate at positions III and IV wherein residues I to IV are positioned substantially the same as residues 108, 42, 39 and 82 respectively in either of SEQ. ID. Nos 1 or 2, or residues 107, 41, 38 and 78 in SEQ. ID. 3 or residues 139, 71, 67 and 112 ~~122, 54, 50 and 95~~ in SEQ. ID. 4, and functional equivalents thereof.
2. (currently amended). A histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than  $10^{-7}M$  and which has a binding site comprising amino acid residues phenylalanine or isoleucine at residue I, tryptophan at residue II and aspartate or glutamate at residues III and IV wherein residues I to IV are positioned substantially the same as residues 98, 137, 24 and 120 respectively in either of SEQ. ID. Nos 1 or 2, or residues 95, 138, 23 and 120 in SEQ. ID. 3 or residues 129, 166, 52 and 152 ~~112, 149, 35 and 135~~ in SEQ. ID. 4, and functional equivalents thereof.
3. (currently amended). A histamine binding compound capable of binding to histamine or serotonin with a dissociation constant of less than  $10^{-7}M$  and which has two binding sites, the first binding site comprising amino acid residues phenylalanine, isoleucine or leucine at position I, tryptophan at position II and aspartate or glutamate at positions III and IV wherein residues I to IV are positioned substantially the same as residues 108, 42, 39 and 82 respectively in either of SEQ. ID. Nos 1 or 2, or residues 107, 41, 38 and 78 in SEQ. ID. 3 or residues 139, 71, 67 and 112 ~~122, 54, 50 and 95~~ in SEQ. ID. 4, and the second binding site comprising amino acid residues phenylalanine or isoleucine at residue I, tryptophan at residue II and aspartate or glutamate at residues III and IV wherein residues I to IV are positioned substantially the same as residues 98, 137, 24 and 120 respectively in either of SEQ. ID. Nos 1 or 2, or residues 95, 138, 23 and 120 in SEQ. ID. 3 or residues 129, 166, 52 and 152 ~~112, 149, 35 and 135~~ in SEQ. ID. 4, and functional equivalents thereof.

4. (currently amended). A histamine ~~binding~~ or serotonin binding compound according to claim 1 or 3 additionally comprising at residue V, a tyrosine residue, wherein residue V is positioned substantially the same as residue 100 in the sequence of either of SEQ. ID. Nos 1 or 2, residue 97 in SEQ ID 3 or residue 114 in SEQ ID 4, and functional equivalents thereof.
5. (original). A histamine or serotonin binding compound according to claim 2 or 3 additionally comprising at residue V, a tyrosine residue, wherein residue V is positioned substantially the same as residue 29 in the protein sequence of either of SEQ. ID. Nos 1 or 2, residue 28 in SEQ ID 3 or residue 40 in SEQ ID 4, and functional equivalents thereof.
6. (previously amended). A histamine or serotonin binding compound according to any of Claims 1, 2 or 3 wherein said compound is stabilised by either or both of the disulphide bridges formed between cysteines 48 and 169 and cysteines 148 and 119 in the protein sequence of either of SEQ. ID. Nos 1 or 2, cysteines 47 and 175 and cysteines 151 and 119 of SEQ ID 3 or cysteines 162 and 134 of SEQ ID 4.
7. (currently amended). A histamine or serotonin binding compound of any one of claims 1, 2 or 3 which comprises a peptide, or a fragment of any one of the proteins FS-HBP1, FS-HBP2, MS-HBP1 or D.RET6.
8. (withdrawn).
9. (withdrawn).
10. (previously amended). The histamine or serotonin binding compound of any one of claims 1, 2 or 3 that comprises a synthetic compound.
11. (previously cancelled).
12. (previously cancelled).
13. (previously cancelled).

14. (previously cancelled).
15. (previously cancelled).
16. (previously cancelled).
17. (previously cancelled).
18. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 produced by recombinant DNA technology.
19. (previously amended). A histamine or serotonin binding compound or protein according to any one of claims 1, 2, 3 or 51 that binds specifically to histamine.
20. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 having an effector or reporter molecule attached thereto.
21. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 that is derived from blood-feeding ectoparasites, spiders, scorpions or snakes and venomous animals.
22. (original). The histamine or serotonin binding compound or protein of claim 21 that is derived from ticks.
23. (original). The histamine or serotonin binding compound or protein of claim 22 that is derived from Ixodid ticks.
24. (original). The histamine or serotonin binding compound or protein of claim 23 that is derived from *Rhipicephalus appendiculatus*, *D. reticulatus*, *Amblyomma variegatum*, *Boophilus microplus* or *Ixodes hexagonus*.
25. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 associated with one or more carbohydrate moieties.

26. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 that is associated with one or more peptides or polypeptides.

27. (original). The histamine or serotonin binding compound or protein of claim 26 that is genetically or chemically fused to one or more peptides or polypeptides.

28. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 attached to a label or toxin.

29. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 that is bound to a support, such as a resin.

30. (previously amended). A therapeutic or diagnostic composition comprising a histamine or serotonin binding compound or protein according to any one of claims 1, 2, 3 or 51.

31. (original). A therapeutic or diagnostic composition according to claim 30 additionally comprising serotonin.

32. (original). A therapeutic or diagnostic composition according to claim 31 additionally comprising a cysteinyl leukotriene, platelet activating factor, or a thromboxane.

33. (previously amended). A vaccine comprising a histamine or serotonin binding compound or protein according to any one of claims 1, 2, 3 or 51.

34. (previously amended). The histamine or serotonin binding compound or protein according to any one of claims 1, 2, 3 or 51 for use in therapy.

35. (previously cancelled).

36. (previously cancelled).

37. (previously cancelled).

38. (previously cancelled).

39. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 for use in the detection or quantification of histamine in human, animal, plant, and food material.

40. (previously amended). The histamine or serotonin binding compound of any one of claims 1, 2, 3 or 51 for use in the depletion or removal of histamine from food products, cell cultures or human, animal, plant and food material.

41. (previously amended). The histamine or serotonin binding compound of any one of claims 1, 2, 3 or 51 for use in the binding or detection of histamine in humans or animals.

42. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 for use as an anti-histamine agent, an anti-inflammatory drug or in the treatment of allergy.

43. (previously amended). The histamine or serotonin binding compound or protein of any one of claims 1, 2, 3 or 51 for use as a tool in scientific research concerning the role of histamine in biological processes .

44. (previously amended). A method for treating or preventing inflammation or allergic reaction in humans or animals, comprising administering a therapeutically effective amount of a histamine or serotonin binding compound according to any one of claims 1, 2, 3 or 51 in conjunction with a pharmaceutically-acceptable carrier.

45. (withdrawn).

46. (withdrawn).

47. (withdrawn).

48. (withdrawn).

49. (withdrawn).

50. (withdrawn).

51. (withdrawn).